A retrospective cohort study comparing the infection rate of COVID-19 in those taking long-term hydroxychloroquine with that of the Welsh general population

Bailie H, Pratt L, Banerjee S

GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Caerdydd a'r Fro
Cardiff and Vale University Health Board

Introduction

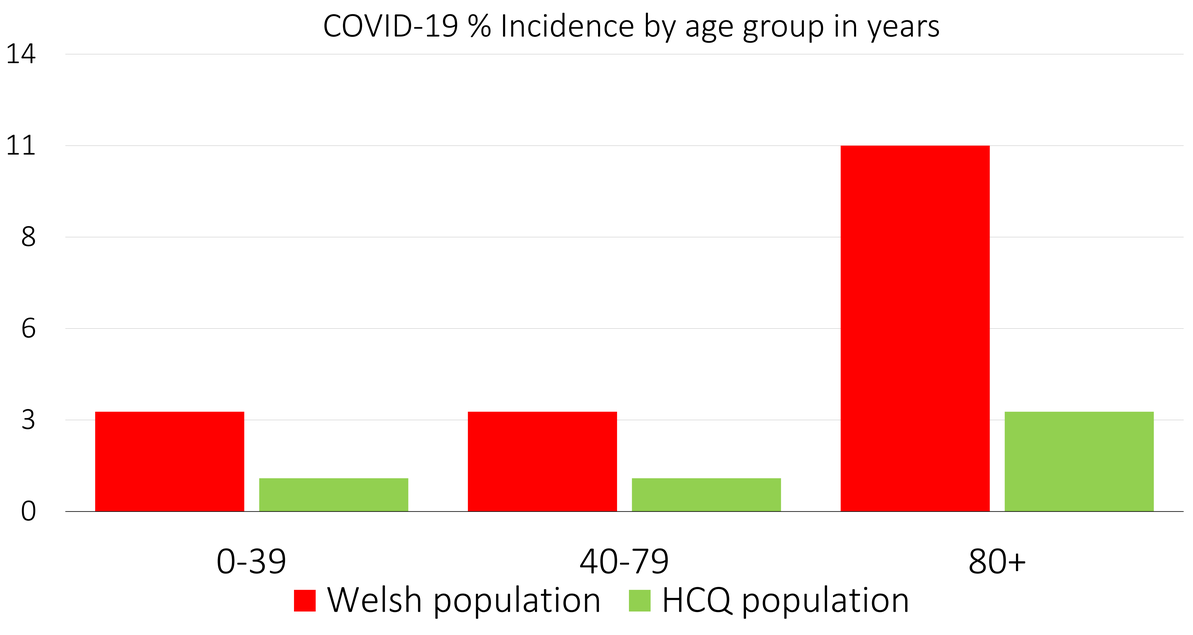
There is a natural subset of ophthalmology patients who take long-term immunosuppressive medications, including hydroxychloroquine (HCQ). This provided an exciting opportunity to collect data on this intriguing group during the COVID-19 pandemic. Although published research to date shows no evidence for HCQ as a treatment for patients who have COVID-19, this leaves open the question whether it has a prophylactic effect against new infections.

Method

We retrospectively collected data from the Cardiff and Vale Health Board from all the patients prescribed HCQ during the period 18th March - 30th June 2020 (n=1099). We compared this data to that provided by Public Health Wales on the Welsh general population of 3,152,879 citizens for the same period. Census data was sourced from the Office of National Statistics.

Results

- 89 COVID-19 tests were conducted in the HCQ population (8%). Of these, 11 were positive (12%), therefore 1% of this population had a positive test for COVID-19.
- When sub-divided by age we found in the HCQ cohort: those aged between 0-39 years; 0.95% tested positive for COVID-19, 0.78% in those 40-79 years, and 3% in those aged 80+.
- Equivalent figures in the Welsh general population were: 2.5%, 3.1% and 10.6% respectively (see graph).



Discussion

COVID-19 is caused by SARS-CoV-2.[1] Early in the pandemic chloroquine and HCQ were reported to be effective against SARS-COV-2.[2] It is known that SARS-COV-2 binds to human cells via the ACE2 receptor. [3,4] The ACE2 receptor is glycosolated by CQ/HCQ in in-vitro studies, inhibiting SARS-COV-2 infection.[5] This led to the possibility of using these drugs in the treatment and even the prophylaxis against COVID-19. HCQ is used in autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis; an immunomodulator.[6]

It is therefore considered that this drug may be effective in reducing the severity of COVID-19 by suppressing the immune system response to SARS-COV-2, which contribute to the severe forms of the disease.[7]

Studies have not found benefit of HCQ as either post-exposure prophylaxis or as a COVID-19 treatment.[8,9,10,11] But there are limited studies investigating the possibility of the use of this medication to prevent COVID-19, or severe outcomes.[12]

Our results show a lower incidence of infection per age-matched groups in those taking HCQ compared to the general population, suggesting there may be a prophylactic-effect against COVID-19 infection.

Although our study suggests a possible protective benefit, due to the observational nature of the study, residual confounding remains a possibility. Moreover, those people who are more severely immunosuppressed or had more co-morbidities might have been more likely shield or adopt more risk avoiding behaviours.

Other studies have not supported the prophylactic benefit of HCQ. In the study by Rentsch et al. their study found no significant difference in COVID-19 mortality associated with HCQ use.[13] Two other RCTs of HCQ for pre-exposure prophylaxis in health-care workers at risk of SARS-CoV-2 infection, found no difference in infection rates.[14,15]

Conclusion

Our study supports that hydroxychloroquine may be associated with some degree of protection against acquiring infection of COVID-19. Further clinical trials as to the prophylactic use of hydroxychloroquine would be warranted.

References

1. Wang,L.,Wang,Y.,Ye,D.&Liu,Q.Review of the2019 novel coronavirus (SARS-CoV-2) based on current evidence.Int.J.Anti- microb. 2020; Agents 55, 105948–105948.
2. Geleris,J.et al. Observational study of hydroxychloroquine in hospitalized patients with Covid-19.N.Engl.J.Med. 2020; 382,2411–2418.
3. Devaux, C.A., Rolain,J.-M.& Raoult, D. ACE2 receptor polymorphism: Susceptibility to SARS-CoV-2, hypertension, multi-organ failure, and COVID-19 disease outcome. J. Microbiol. Immunol. Infect. 2020; 53, 425–435.
4. Pahan, P. & Pahan, K. Smooth or risky revisit of an old malaria drug for COVID-19?. J. Neuroimmune Pharmacol. 2020; 15, 174–180.
5.Yao X Ye F Zhang M et al.In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clin Infect Dis. 2020; 71: 732-739
6. Schrezenmeier, E. & Dörner, T. Mechanisms of action of hydroxychloroquine and chloroquine: Implications for rheumatology. Nat. Rev. Rheumatol. 2020; 16, 155–166. https://doi.org/10.1038/s41584-020-0372-x.
7. Pahan, P. & Pahan, K. Smooth or risky revisit of an old malaria drug for COVID-19?. J. Neuroimmune Pharmacol. 2020; 15, 174–180.
8.Boulware DR Pullen MF Bangdiwala AS et al.A randomized trial of hydroxychloroquine as postexposure prophylaxis for Covid-19. N Engl J Med. 2020; 383: 517-5259.
9. Skipper CP Pastick KA Engen NW et al.Hydroxychloroquine in nonhospitalized adults with early COVID-19: a randomized trial. Ann Intern Med. 2020; 173: 623-631
10.COVID19 Clinical Trials Report Card: Chloroquine and hydroxychloroquine—CEBM. https://www.cebm.net/covid19/ covid19clinicaltrialsreportcardchloroquineand hydroxychloroquine/ (accessed Oct 6, 2020).
11.The RECOVERY Collaborative Group. Effect of hydroxychloroquine in hospitalized patients with Covid19. N Engl J Med 2020.
12.Hernandez AV, Roman YM, Pasupuleti V, Barboza JJ, White CM. Hydroxychloroquine or chloroquine for treatment or prophylaxis of COVID19: a living systematic review. Ann Intern Med 2020; 173: 287–96.
13.Rentsch CT DeVito NJ MacKenna B et al. Effect of pre-exposure use of hydroxychloroquine on COVID-19 mortality: a population-based cohort study in patients with rheumatoid arthritis or systemic lupus erythematosus using the OpenSAFELY platform. Lancet Rheumatol. 2020; 3,19-27
14.Abella BS Jolkovsky EL Biney BT et al.Efficacy and safety of hydroxychloroquine vs placebo for pre-exposure SARS-CoV-2 prophylaxis among health care workers: a randomized clinical trial.JAMA Intern Med. 2020;
15.Rajasingham R Bangdiwala AS Nicol MR et al.Hydroxychloroquine as pre-exposure prophylaxis for COVID-19 in healthcare workers: a randomized trial. Nephrol Dial Transplant. 2020